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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/513,151 | 02/25/2000 | Siegfried Hekimi | 979-1-017 | 7817 |

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|---|
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| ART UNIT | PAPER NUMBER |
|---|---|
| 1642 | |

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Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

| Application No. | Applicant(s) |
|---|---|
| 09/513,151 | Hekimi et al |
| **Examiner** | **Art Unit** |
| Karen Canella | 1642 |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3 months* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☐ Responsive to communication(s) filed on _____.

2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above, claim(s) *7-20* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-6* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
18) ☐ Interview Summary (PTO-413) Paper No(s). _____
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

***Response to Amendment***

1. Claim 1 has been amended. Claims 1-20 are pending. Claims 7-20, drawn to non-elected inventions, remain withdrawn from consideration. Claims 1-6 are under consideration.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

3. Acknowledgment is made of applicants request for rejoinder of all pending claims. However, the restriction requirement was made final in the Office action of Paper No. 8. Applicant is referred to the MPEP (1.144) which states:

> After a final requirement for restriction, the applicant, in addition to making any reply due on the remainder of the action, may petition the Commissioner to review the requirement. Petition may be deferred until after final action on or allowance of claims to the invention elected, but must be filed not later than appeal.

4. The specification is objected to as not complying with 1.821(d) of the Sequence Rules and Regulations. When the specification of a patent application discusses a sequence listing that is set forth in the "Sequence Listing" in accordance with paragraph (c ) of the Sequence Rules and Regulations, reference must be made to the sequence by use of the assigned identifier, in the text of the description or claims of the patent application. The specification and figures abound with recitation of gro, gop and hap genes and proteins and DNA and amino acid sequences arising from a multiplicity of organisms without sequence identifiers.

Appropriate correction is required.

***New Grounds of Rejection***

5. Claims 1-5 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is indefinite in the recitation of "functional fragments" as it does not define what the claimed function consists of. For purpose of examination, the claimed function will be the same as the wild-type gro-1 gene.

Claim 2 is vague and indefinite in the recitation of figures 9A-9B as a sole means of identifying an amino acid sequences. The MPEP (2173.05(s)) states: Where possible, claims are to be complete in themselves. Incorporation by reference to a specific figure or table "is permitted only in exceptional circumstances where there is no practical way to define the invention in words and where it is more concise to incorporate by reference than duplicating a drawing or table into the claim. Incorporation by reference is a necessity doctrine, not for applicant's convenience." Ex parte Fressola, 27USPQ2d 1608, 1609 (Bd. Pat. App. & Inter. 1993)

Amendment of the claim to incorporate the appropriate sequence identifier of the amino acid sequence is recommended.

6. Claims 1-6 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Amendment of the claims to recite isolated genes is recommended.

7. Claims 1-6 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.
(A)As drawn to the human homologs of the gro-1 and hap-1 genes of C elegans

Claim 1 is drawn to the polynucleotide of SEQ ID NO:3 which is the human homolog of the C elegans gro-1 gene. Claim 2 is drawn to the gene which codes for the protein set forth in figures 9A-9B. Claim 7 is drawn to the polynucleotide of SEQ ID NO:7 which is the human homolog of the C elegans hap-1 gene. The specification teaches that the gro-1 gene and related genes are located in the gro-1 operon and express proteins that function at the level of cellular physiology and developmental rate and aging in C. Elegans. The specification teaches that the gro-1 genes are isolated from C. Elegans and that worms harboring a mutation in gro-1 (the e2400 mutation) have a longer life and an altered cellular metabolism relative to the wild type.

The specification teaches that the predicted amino acid sequence encoded by the gro-1 transcript is highly similar to dimethylallyltransferase (pg. 13, lines 20-24) found in E. Coli and S. Cerevisiae. However, neither the specification nor any art of record teaches the properties of the human gro-1 or hap-1 proteins or the functioning of the gro-1-1 polypeptide as a mediator of development and aging in humans, or as a mediator in any other human disease. The specification provides no objective evidence that human individuals with a longer lifespan have mutations in the gro-1-1 protein or genes contributing to their longevity. The specification provides no objective evidence that induction of a mutation in a gro-1 gene can inhibit tumor growth. Furthermore, based on the similarity of gro-1 to dimethylallyltransferase, one of skill in the art would not know how to use the claimed gro-1 genes to alter longevity or to treat cancer as there is no direct relationship between dimethylallyltransferase and the cancerous state. Although gro-1 is a conserved gene in bacteria and lower eukaryotes, it does not necessarily follow that it is responsible for the same phenotype in higher mammals as in nematodes. Applicant has argues that there are numerous examples in the art where proteins carrying out similar biochemical functions in different genuses have similar effects on the organism. Applicant points out that the CED protein in C elegans and the Bcl-2 human protein have conserved function between human and nematode as both proteins function in the regulation of apoptosis. Applicant further argues that the human Bcl-2 can function in the nematode and exert the same anti-apoptotic effect and that the post-filing reference, Golovko et al, teaches that the human gro-1 gene can function in yeast mutants lacking the wild-type gene. These arguments have been considered but not found persuasive. The effect of an enzyme on a single cell or a simple organism such as C elegans can be anticipated, however, the effect of an enzyme on a complex multicellular organism cannot be construed solely from experiments on C elegans. Alberts (Molecular biology of the Cell, 1989, page 902) teaches that " the behavior of a cell at any time will generally depend on the choices made by its ancestors in the previous division cycles.....in vertebrates and many other organisms the details of cell lineage show random variations, even between genetically identical animals", Thus Alberts et al teaches that the history of cell-cell interactions in higher organisms determine cell fate in addition to the biochemistry of a single cell. Further Alberts et al teaches "In some

lower phyla, including mollusks, annelids and nematode worms, the divisions and movements of individual cells are ordered with extreme precision and in an almost identical way in each member of the species....Against this background, the effects of mutations ...can be pinpointed very precisely", thus, it is recognized in the art that complex factors such as cell-cell interactions which play a large part in the determination of cellular fate in higher organisms are simplified in C elegans. Without further teaching and guidance from the specification, one of skill in the art would be subject to undue experimentation in order to use the claimed teachings regarding the gro-1-1 (SEQ ID NO:3) and hap-1 (SEQ ID NO:7) polynucleotide on complex multicellular vertebrates such as humans as the function of human homolog cannot be anticipated based on the function of the C elegans genes.

(B)As drawn to functional fragments of human gro-1

Claim 1 is drawn in part to functional fragments of the human gro-1 gene. The claim does not specify what said "function" is intended. The specification describes a method for the screening of functional fragments of the C elegans gro-1 gene based on a rescue of the e2400 mutant phenotype which exhibits a reduced rate of development and aging. The specification does not describe a method or assay to determine or screen for functional fragments of the human gro-1 gene. Further, one of skill in the art would be subject to undue experimentation in order to find functional fragments of the claimed gene as the function of the entire gene has not be demonstrated.

(c)As drawn to hap-1, gop-1, gop-2 and gop-3

Due to the absence of critical sequence identifiers in the specification, the species origin of the gop genes cannot be determined with absolute certainty. Because of the claimed presence of gop genes in an operon, it is assumed for purpose of examination that gop-1, 2 and 3 are C elegans genes. The human hap-1 gene of SEQ ID NO:7 is not enabled for the reasons stated in section A, above. In addition, the specification teaches that the hap-1 gene is the same as the ZC395.7 clone (page 13, lines 13-15) which was not capable of rescuing the e2400 mutant (figure 2B and page 10, lines 18-20) when present in the pMQ4 construct. Therefore, the ZC395.7 subclone is not important to the function of the gro-1 gene. Therefore there is no basis for

inferring that the hap-1 gene is important for the functioning of the gro-1 gene. The hap-1 gene is part of the gro-1 operon from which gop-1, 2 and 3 are also transcribed. However, the specification does not teach how to use the gop proteins from C elegans or the hap-1 protein as they do not participate in rescuing the wild type gro-1, nor do they encode another functional protein. One of skill in the art would be subject to undue experimentation in order to practice the claimed invention.

***Conclusion***

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen Canella whose telephone number is (703) 308-8362. The examiner can normally be reached on Monday through Friday from 8:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on (703) 308-3995. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

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Karen A. Canella, Ph.D.
Patent Examiner, Group 1642
March 18, 2002